THE RESISTANCE OF DIABETICS TO BACTERIAL INFECTION.

A STUDY OF THE OPSONOPHAGOCYTIC PROPERTIES OF THE BLOOD IN 74 CASES OF DIABETES MELLITUS AND RELATED CONDITIONS.[1]

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Diabetes mellitus, always an inviting field for research, appears to offer particularly attractive possibilities in connection with its bearing upon the opsonic properties of the blood, which, it seems reasonable to presume, should be more or less influenced by the pronounced metabolic disturbances incident to this disease. Especially is this true of cases attended by excessive glycosuria, and of those characterized by glaring inadequacy of fat oxidization, whereby the acetone bodies accumulate unduly in the blood and in the other tissues of the body, thus rendering the subject prone to the dangers of acid intoxication. The well-recognized susceptibility of the diabetic individual to boils and carbuncles, to spontaneous gangrene, and to pulmonary tuberculosis also argues, on *a priori* grounds, some deviation from the normal opsonin values, either as a cause or as a consequence of these complications. Furthermore, one is tempted to accept as more than an alluring theory a possible relation between the opsonic function and the hormone body "secretin;" which substance, having been proved by Bayliss and Starling[2] to be an active factor of pancreatic secretion, was found to exist in minimal quantities in the non-pancreatic type of diabetes by Bainbridge and Beddard,[3] and more recently has been studied by Wentworth,[4] and by Sweet and Pemberton,[5] with relation to diabetes and other states of defective nutrition.

With the foregoing premises in mind, we have thought it worth while to investigate, in a reasonable number of diabetic subjects, the condition of the hemic resisting powers, as reflected by the behavior of the opsonic and phagocytic values in the individual instance. It is aside from the main question here to interpret the significance of opsonins and their effects upon the mechanism and other phases of bacterial invasion, and for information about these fundamental details original sources should be consulted.[6] It is sufficient for the purposes here served to note that it is justifiable to regard opsonins as substances native to normal blood plasma which act upon various invading bacteria so as to render them easily phagocyted by the leukocytes; it is also probable that the erythrocytes are prepared for phagocytosis in an analagous manner, by the effect of the so-called "hemopsonin" of the blood; and a similar crippling of certain animal parasites—notably the trypanosome and the spirochete of relapsing fever—is believed to occur as an act preparatory to the engulfment of these microörganisms by phagocytes.

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[1] Read at a meeting of the Section on General Medicine of the College of Physicians of Philadelphia, March 9, 1908.

[2] Jour. Amer. Med. Assoc., 1907, xlviii. 524.

[3] Biochem. Jour., 1906, i. 429.

[4] Jour. Amer Med. Assoc., 1907, xlix, 204.

[5] Arch. Inter. Med., 1908, i, 231.

The present series of 52 cases is a supplement to the 22 reported by one of us (Da C.) a year ago, as a preliminary record of "The Opsonic Index in Diabetes Mellitus,"[7] which showed that in this disease the subject's opsonic powers are appreciably diminished, in comparison with those of a normal person, while in diabetes insipidus and in conditions of transient glysocuria no such deviation can be distinguished. The combined series of 74 cases, herewith reported, includes 50 examples of true diabetes mellitus, 4 of diabetes insipidus, 8 of non-diabetic glycosuria, and 12 of furunculosis and acne unattended by glycosuria. The data relating to this series is based upon 850 direct and control blood examinations, plus numerous repeated tests, bringing the total number of examinations close to the thousand mark. Most of the clinical material was supplied by the Jefferson, the German, and the Philadelphia General Hospitals, but for a number of referred patients we are indebted to several medical friends, especially to Dr. O. H. Petty, Dr. S. A. Munford, and Dr. J. H. Gibbon. The technical part of the work was done, through the courtesy of Prof. H. A. Hare, in his Laboratory of Clinical Medicine and Therapeutics at the Jefferson Medical College Hospital.

In the report just alluded to, it was shown that a diabetic's opsonic index to Staphylococcus pyogenes is subnormal; in this new group of 34 patients we have continued our studies with this bacterium, and, in addition, sought to determine the behavior of the blood opsonins in connection with two other varieties of bacteria, Streptococcus pyogenes and Bacillus tuberculosis. These microörganisms were selected as test-bacteria on the assumption that to such sources of infection the diabetic is peculiarly susceptible, and in this connection it may be noted that in 56 per cent. (28 cases) of our diabetic patients complications traceable to these germs existed.

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[6] These contributions give the essential data and the literature of opsonins and the diagnostic and therapeutic application of the opsonic theory: Wright and Douglass, Proc. Roy. Soc., 1903, lxii, 357; Ibid., 1904, lxiii, 128, 135, 147; Wright, Lancet, 1907, ii, 423, 1213; Ross, Brit. Med. Jour., 1906, ii, 1452; Jour. Amer. Med. Assoc., 1907, xlix, 245; Craco-Calvert, Lancet, 1907, i, 279; French, Brit. Med. Jour., 1907, i, 256, 862; Ehrlich, Lancet, 1907, i, 279; Simon and Lamar, Johns Hopkins Hosp. Bull., 1906, xvii, 27; Hektoen and Reudiger, Jour. Infect. Dis., 1905, ii, 128; Potter, Ditman, and Bradley, Jour. Amer. Med. Assoc., 1906, xlvii, 1722, 1793; Miller, Ther. Gaz., 1907, xxx, 173.

[7] AMER. JOUR. MED. SCI., 1907, cxxxiv, 57.

TECHNIQUE. The technique used in all our estimations was essentially that of Wright,[8] with certain modifications of minor importance suggested by our increasing familiarity with the work, bred of some eighteen months experience with it. But in addition to computing merely the opsonic index to the three types of bacteria mentioned, we have also determined, in each of the new patients, the number of phagocytes in a given number of leukocytes, as well as the number of bacteria adherent to, although not actually engulfed by, the leukocytes, irrespective of their phagocytic proclivities. Thus the opsonizing properties of the blood plasma are indexed by the first process, the proportion of potential phagocytes is calculated by the second, while the last procedure may have, we fancy, some more or less close relation to the one immediately preceding.

The method of calculating the ordinary opsonic index is now so well known that it is unnecessary to recount the details in this place. Those interested will find a description of our technique in an (Da C.) article in this Journal for July, 1907.[9] It may, however, be noted that, for the sake of uniformity, only polynuclear neutrophile leukocytes were counted as phagocytes, since this rôle is so infrequently and so indifferently assumed by large mononuclear leukocytes that, to all intents and purposes, they are a negligible quantity in opsonophagocytic estimates.[10]

The richness of the blood in phagocytes was studied by ascertaining their percentage in the patients' blood, and by comparing this value with a corresponding value for normal blood (considered as 1), thus obtaining a figure that may be expressed as the "phagocytic index." Under the term "percentage index" Simon has described in detail this method of research.[11]

Our object in taking account of the attached or attracted bacteria was to discover what bearing, if any, such a condition has on true phagocytosis. Having repeatedly observed specimens of blood containing few phagocytes, but many leukocytes with numerous bacteria tightly adherent to their peripheries, this question arose: Does such a picture mean actual crippling of the cells' phagocytic powers, whereby bacteria are apparently attracted, but not engulfed; or can it be explained simply by some coincidence, or by an error in technique, such as, for example, the use of a rich, unhomogeneons culture? These questions will be discussed presently. Provisioually, the term "index of attracted bacteria" is useful to designate the figure obtained by comparing the number of leukocytes with adherent bacteria in diabetic and in normal bloods, using 1 as the normal standard.

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[8] Loc. cit.

[9] Loc. cit.

[10] In less than 3 per cent. of our examinations did this type of cells figure as phagocytes, and then only in small numbers—two or three to each count of 50 leukocytes.

[11] Jour. Amer. Med. Assoc., 1907, xlviii, 139.

In the following account of our experimental work we shall analyze the results according to these three groups of cases:

I. Diabetes mellitus.
II. Diabetes insipidus.
III. Non-diabetic glycosuria.

I. DIABETES MELLITUS. Of this affection 50 cases have been examined, all of which were undoubtedly true diabetes mellitus, as proved by the clinical history and by the urine analysis. In the 34 diabetics of the second series the frequency of the most prominent symptoms at the time of the blood examination may be tabulated thus:

	Per cent.	Cases.
Polyuria	91.1	31
Abnormal thirst	85.2	29
Wasting	82.3	28
Excessive appetite	70.5	24
Furunculosis	52.9	18
Pulmonary tuberculosis	29.3	10
Coma	5.8	2

Glycosuria was found in all the patients, but in none was the sugar-content excessive, ranging from as low as 0.3 per cent. to as high as 3.4 per cent. This peculiarity was probably due to the fact that the great majority of the subjects were on strict diet and systematic medical treatment, either at the out-patient clinic or in the hospital ward. Acidosis was found in 44.4 per cent. (15 cases), and albuminuria in 41.4 per cent. (14 cases) of the patients examined. No lesion of the pancreas or of the liver was found in any of the patients.

In the foregoing group the opsonic index to Staphylococcus was determined in 50, while the indices to Streptococcus and to Bacillus tuberculosis were computed in the 34 patients of the new series only. In all the latter the values relating to phagocyted and attracted bacteria were also obtained. The information derived from this inquiry makes these conclusions inevitable:

(a) Diabetics, as a class, have subnormal *opsonic indices* to Streptococcus, Staphyloccus, and Bacillus tuberculosis, the diminution being most striking in tests made with the first-named bacterium, well defined with the second, and moderate with the last (Chart I).

As shown by Table I, the streptococcus index averaged 44 points below the accepted normal figure, ranging between 0.38 and 1.0, and falling below 0.5 in 7 tests. The staphylococcus index, although averaging 9 points higher than this, fell below 0.5 in 16 examinations; while the tubercle index, which averaged 17 points higher than the streptococcus value, fell below 0.5 but 3 times. Comparing the most common index-range of these three bacteria (that is, 0.5 to 1.0), a much better conception of their relative values is possible, this analysis showing these averages:

Staphylococcus:	0.66, average index for 33 cases.
Streptococcus:	0.66, " " " 29 "
Tubercle bacillus:	0.65, " " " 24 "

TABLE I.—ANALYSIS OF THE INDICES IN 50 CASES OF DIABETES MELLITUS.[12]

	Opsonic Index.			Phagocytic Index.			Index of Attached Bacteria.		
	Staph.	Strep.	T. B.	Staph.	Strep.	T. B.	Staph.	Strep.	T. B.
Average	0.65[13]	0.56	0.73	0.74	0.64	0.70	0.50	0.47	0.59
Maximum	1.44	1.00	1.73	1.18	1.04	1.33	2.64	3.00[14]	8.30[15]
Minimum	0.25	0.38[16]	0.45	0.25	0.11[16]	0.20	0.16[16]	0.10	0.10
Range of Indices.									
No. above 1.0 . . .	1	0	2	3	1	2	3	1	1
No. 0.5 to 1.0 . . .	33	26	29	26	26	25	6	10	7
No. below 0.5 . . .	16	8	3	5	7	7	25	23	26

(*b*) The *phagocytic* and opsonin values are closely parallel with Bacillus tuberculosis, the former averaging 0.70 and the latter 0.73 in 34 experiments conducted with this germ (Chart II). With Streptococcus, however, the relation is not so close, averaging as 0.64 is to 0.56; and with Staphyloccus the breach is still wider—as 0.74 is to 0.65.

These departures of the phagocytic and the opsonic indices are most difficult to explain, although most of them can safely be referred to technical defects inherent to the tests. The propinquity of the bacteria to the cells, variations in the richness of the bacterial emulsion—not to mention personal errors in technique, apparently unavoidable—are doubtless often to blame. But such questions are not germane to our subject-matter, and their discussion must raise anew the controversy as to the relative value of the act of phagocytosis, and its result as gauged by the actual number of bacteria within the cells. In passing, it may be said that neither index should be considered a strictly quantitative guide, but a qualitative figure. The value of an opsonic index relates not to the precise figure registered thereby, but rather to the finding of a decided deviation from normal; and in the moderately subnormal ranges one may not hazard a definite conclusion, although at both extremes the readings are significant.

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[12] Staphylococco-index in 50 cases; streptococco- and tuberculo-indices in 34.

[13] In 34 cases of second series=0.63 for average streptococco-opsonin index.

[14] In 7 cases no attached bacteria observed.

[15] In 4 cases no attached bacteria observed.

[16] In 3 cases no phagocyted streptococci found; no attached bacteria.

(c) The *index of attached bacteria*, or those adherent to the periphery of the leukocytes, was studied with especial care in 34 bloods, in the hope of discovering some connection between this phenomenon and that of phagocytosis (Chart III). But the variations in our results were so wide that it is impossible definitely to associate the two processes: some actively phagocytic bloods contain leukocytes with no adherent bacteria whatever, while in others just the opposite is observed. It is tempting to explain the former circumstance by assuming therein an extraordinary leukocytic defence, and the latter by assuming deficiency of this power, although it is saner to reject both hypothesis, leaving the question open to discussion. Three facts, however, were brought out by studying this detail of the attached bacteria: (1) That of the three different bacteria employed, tubercle bacilli were most frequently found clinging to the leukocytes, and, as a rule, doing so in far greater numbers than either strepto-

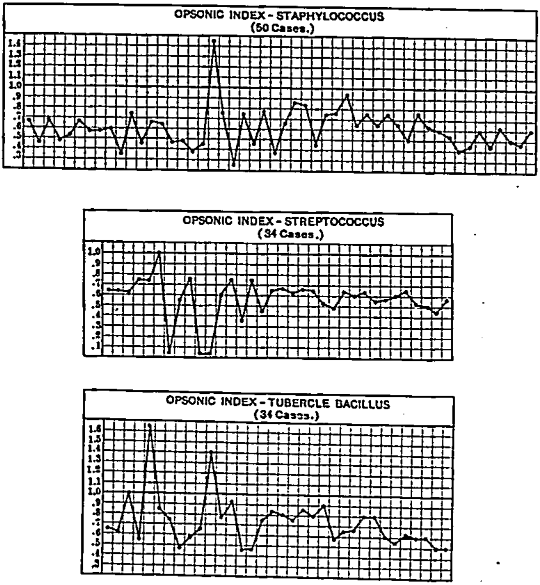

Chart I.—Opsonic indices in diabetes mellitus.

cocci or staphylococci; (2) that in the lower ranges (below 0.5) the uniformity of the index for all three bacteria was practically constant, differing, but very slightly, in favor of the tubercle bacillus; and (3) that to a somewhat less degree the same is true of the range of averages between 0.5 and 1.

The points referred to in the three preceding paragraphs are well illustrated by Table I, and in the accompanying charts the individual ranges of the three different indices are shown.

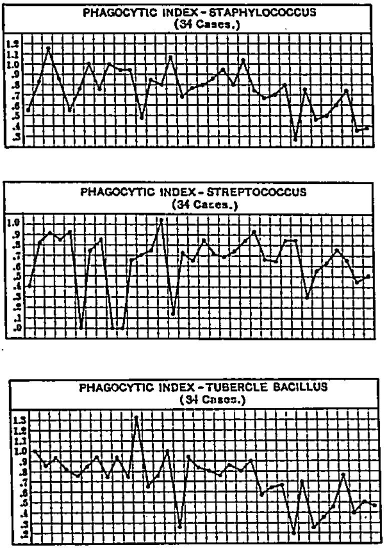

Chart II.—Phagocytic indices in diabetes mellitus.

(*d*) *Influence of Complications.* Thus far we have considered diabetics as a class, aside from which there remain numerous cases to be reviewed comparatively, owing to the existence of certain well-marked attendant or complicating conditions. To this class, then, belong those with acidosis, those suffering from furunculosis, and those affected with tuberculosis of the lungs.

In the group of *diabetes with acidosis* are included 15 patients whose urine contained acetone, diacetic acid, or both, in appreciable

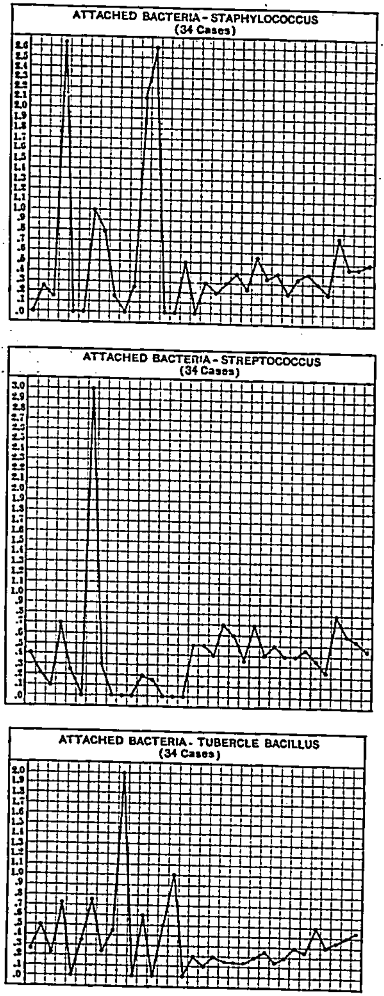

Chart III.—Indices of attached bacteria in diabetes mellitus.

amount at the time of the blood examination.[17] The term "acidosis" is used, therefore, in a somewhat loose sense, rather than necessarily to denote frank acid intoxication, perhaps amounting to coma, which was present in but two instances.

In dealing with this class of examinations one is forcibly impressed with two findings: the unduly low tubercle indices, both opsonic and phagocytic, in comparison with similar figures for cases without acidosis; and the virtually constant correspondence of the streptococcus and staphylococcus values in the two groups of patients.

Thus, the tuberculo-opsonic index averaged 23 points lower, and the tuberculophagocytic index 19 points lower, in acidosis cases than in the non-acidosis class. Even the questionable index of attracted bacteria declined in a most extraordinary degree—62 points for tubercle, and from 30 to 40 for the other bacteria. With reference to these findings it is important to note that but 2 of the low tuberculo-indices were found in tuberculous subjects affected with acidosis (Cases XXV and XLVII), and in neither was the value of such a nature as materially to affect the averages calculated for the complete acidosis series. In contrast to these deviations, the acidosis group of opsonic and phagocytic indices to the pyogenic cocci closely agreed with like values for patients without acidosis, the two differing not more than 4 points, save in the streptococcus phagocytic index, which ran 10 points lower in the acidosis class.

Of the 2 patients with *diabetic coma*, the urine of the first (Case III) contained both acetone and diacetic acid, and the urine of the second (Case XV) only acetone. In the first instance the opsonic values were 0.44, 0.61, and 0.51 to Staphylococcus, Streptococcus, and Bacillus tuberculosis, respectively; while in the second instance the corresponding values read 0.77, 0.45, and 0.46. In both patients the disease was of the acute type, and in the first one it proved fatal within a fortnight after the subject first came under observation.

This table of averages in diabetes with and without acidosis is illustrative of the decided differences here existing.

TABLE II.—DIABETES MELLITUS WITH ACIDOSIS.

	19 cases without acidosis.[18]	15 cases. with acidosis.
Opsonic index.		
Staphylococcus	0.59	0.63
Streptococcus	0.63	0.60
B. Tuberculosis	0.89	0.66
Phagocytic index.		
Staphylococcus	0.82	0.80
Streptococcus	0.74	0.64
B. Tuberculosis	0.86	0.67
Index attached B.		
Staphylococcus	0.71	0.30
Streptococcus	0.63	0.33
B. Tuberculosis	0.92	0.30

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[17] Lieben's and Gerhardt's tests were used in the routine examinations for acetone and diacetic acid, respectively.

[18] Staphylococco-opsonin index in 35 cases; all others in 19.

Furunculosis was present in 18 of the diabetic subjects, but, aside from certain minor details, this complication seems, *per se*, to have no material effect upon either the opsonic or the phagocytic power of the blood. In furunculosis cases, as well as in those with a clean skin, these averages were not dissimilar, save for a relatively feeble phagocytic action toward the staphylococcus and a comparatively vigorous attack upon the streptococcus, in the former group. In all the experiments it appeared that the combative powers of the leukocytes outstripped their destructive capacity for the bacteria attacked, since the phagocytic index consistently ran somewhat higher than the opsonic figure. The low range of the tubercle index of attached bacteria (45 points subnormal) is here almost as conspicuous as in the acidosis group. Table III demonstrates this peculiarity, as well as the other details just described.

TABLE III.—COMPARATIVE AVERAGE VALUES IN DIABETICS WITH AND WITHOUT FURUNCULOSIS.

	18 diabetics with furunculosis.	16 diabetics without furunculosis.
Opsonic index.		
Staphylococcus	0.62	0.59
Streptococcus	0.59	0.52
B. Tuberculosis	0.69	0.77
Phagocytic index.		
Staphylococcus	0.67	0.82
Streptococcus	0.73	0.53
B. Tuberculosis	0.71	0.78
Index attached B.		
Staphylococcus	0.50	0.51
Streptococcus	0.40	0.55
B. Tuberculosis	0.36	0.91

Apropos of the above results (Table III), it may be noted that in 4 non-diabetic patients with furunculosis the opsonic index to Staphylococcus averaged only 0.45; while in 8 cases of pustular acne (also non-diabetic) the average indices were 0.50, 0.95, and 1.03 to Staphylococcus, to Streptococcus, and to Bacillus tuberculosis, respectively. These data, although limited, emphasize the great decline of the tuberculo-indices in diabetes complicated by furunculosis, in comparison with similar values found in non-diabetic persons affected with pustular lesions.

In *diabetes complicated by pulmonary tuberculosis* both opsonic and phagocytic indices averaged practically the same as those of non-tuberculous diabetics, except for a five-point and a twelve-point variation with the streptococcus. This can probably be disregarded, in view of the trifling differences involved, and because of the consistent uniformity of the other estimates. It is of some interest to find that in tuberculous diabetics the tuberculo-index of attached bacteria falls as it does in acidosis cases, although the average decline is some 11 points less than in the latter. The behavior of the several index averages in tuberculous and non-tuberculous patients is shown by Table IV.

TABLE IV.—DIABETES MELLITUS WITH PULMONARY TUBERCULOSIS.

	24 non-phthisical cases.[19]	10 phthisical cases.
Opsonic index.		
Staphylococcus	0.62	0.61
Streptococcus	0.55	0.60
B. Tuberculosis	0.73	0.75
Phagocytic index.		
Staphylococcus	0.74	0.74
Streptococcus	0.62	0.74
B. Tuberculosis	0.68	0.69
Index attached B.		
Staphylococcus	0.49	0.54
Streptococcus	0.42	0.60
B. Tuberculosis	0.71	0.41

(e) *Influence of Glycosuria.* The relation between the *degree of glycosuria* and the opsonophagocytic action was investigated in every case belonging to the second series, of which 18 had a sugar-content below 5 grains to the ounce, while in 16 this figure was exceeded, the average amount of sugar being 2.1 grains in the first, and 8.3 grains in the second, group.[20] Comparison of these groups admit of but one deduction: that a *high* degree of glycosuria implies a *low* grade of bacterial resistance, while with a moderate glycosuria the index is unquestionably higher. This is emphatically true of the tuberculo-indices, which in patients with a low sugar content showed an opsonic index 29 points higher, and a phagocytic index 33 points higher, than the corresponding value for subjects having a high content of sugar.[21] And here, as in the other cases referred to, the peculiar behavior of the tubercle index of attached bacteria attracts attention, for this value differs no less than 39 points in favor of the "low sugar" group of patients.

TABLE V.—INFLUENCE OF GLYCOSURIA ON THE INDICES.

	18 low sugar cases.[22]	16 high sugar cases.[23]
Opsonic index.		
Staphylococcus	0.66	0.62
Streptococcus	0.69	0.55
B. Tuberculosis	0.89	0.60
Phagocytic index.		
Staphylococcus	0.82	0.76
Streptococcus	0.78	0.64
B. Tuberculosis	0.93	0.60
Index attached B.		
Staphylococcus	0.45	0.64
Streptococcus	0.64	0.36
B. Tuberculosis	0.81	0.42

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[19] Staphylococco-opsonin index in 40 cases; all others in 24.

[20] Fehling's and Böttger's tests were used for glucose, and in doubtful reactions, the fermentation and the phenylhydrazin tests.

[21] The adjectives "low" and "high" here refer to the two degrees of glycosuria above alluded to—those below and those above 5 grains to the ounce.

[22] Four cases with acidosis.

[23] Seven cases with acidosis.

So far as we were able to determine, *albuminuria* is not to be regarded as a factor of index deviations. Nor could any correspondence be recognized between the *leukocyte count* and the phagocytic activity of the cells.

II. Diabetes Insipidus. In 4 cases of diabetes insipidus opsonic indices of 0.82, 0.82, 0.87, and 0.89 to Staphylococcus were found, or values ranging within normal limits, which vary from 0.80 to 1.2, according to Bulloch's studies of 84 healthy subjects.[24] The foregoing cases belong to the first series reported, in which only the staphylococco-opsonic index was investigated, and having met with no more examples of this disease during the past year, we are denied the opportunity of recording the behavior of the phagocytic percentage and the index of attached bacteria in non-saccharine diabetes. On clinical grounds, it is unlikely that there is any deviation from normal, although no actual proof of this presumption is at hand.

III. Non-diabetic Glycosuria. In 8 patients with transient glycosuria all the index values, collectively and individually, were well within the normal range, except in the last 3 tests with Streptococcus, which showed moderately subnormal opsonic indices (0.70, 0.76, and 0.75), with most divergent values for phagocytes. This we regard as a discrepancy due to the use of an unsatisfactory streptococcus culture, with which bacterium, it may be added, we have had considerable trouble at different times. This being the case, we prefer to draw no conclusions from the streptococcus values in the cases under discussion, and figures relating to this germ are stated with this proviso.

With the other bacteria consistently high values were obtained, ranging some 20 to 30 points higher than similar values for diabetes mellitus. Although 8 records are scarcely comparable with 50, we tabulate the averages of non-diabetic glycosuria with those of diabetes mellitus, in view of the striking contrast thereby shown.

Table VI.—Glycosuria versus Diabetes.

	8 glycosuria cases.	50 diabetic cases.
Opsonic index.		
Staphylococcus	0.96	0.65
Streptococcus	0.81 (?)	0.56
B. Tuberculosis	0.98	0.73
Phagocytic index.		
Staphylococcus	1.01	0.74
Streptococcus	1.02 (?)	0.64
B. Tuberculosis	0.93	0.70
Index attached B.		
Staphylococcus	0.79	0.50
Streptococcus	0.62 (?)	0.47
B. Tuberculosis	0.54	0.59

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[24] Trans. Path. Soc., London, 1905, lvi, 334.

CONCLUSIONS. With no sacrifice of logic, we believe that the following deductions are warranted by the clinical and laboratory findings herewith reported:

1. In diabetics, as a class, the resisting powers of the blood against bacterial infection are conspicuously subnormal, in comparison with a similar hemic property in the healthy individual. As measured by the opsonic index, the average diabetic's resistance is approximately one-third below normal, and, in the exceptional case, reduced more than two-thirds. This applies to infections by the streptococcus, the staphylococcus, and the bacillus of tuberculosis, whose relative predilection for the diabetic is expressed by the order given.
2. The higher grades of diabetic glycosuria are attended by a feebler opsonophagocytic action than the lower grades, and the reverse of this also is true. This deficiency is particularly striking in the case of the tubercle bacillus.
3. Diabetic acidosis particularly lowers the blood resistance to the bacillus of tuberculosis, but a less degree of vulnerability appears to exist with regard to the streptococcus and the staphylococcus.
4. Diabetic furunculosis does not materially depress the subject's opsonophagocytic powers to the ordinary pyogenic cocci below the figures usually incident to this disease.
5. Diabetics affected with pulmonary tuberculosis show virtually the same resisting powers as do subjects of uncomplicated diabetes.
6. In non-saccharine diabetes the opsonic values to the staphylococcus range within normal limits, and this statement also applies to non-diabetic glycosuria.

In conclusion, we would advise the use of the opsonic test in diabetes mellitus as a means of gaging, in a general way, the extent to which the subject's vitality is undermined, and for this purpose the test is especially useful in patients threatened with acid intoxication, and in those having excessive glycosuria. Systematic opsonic records in an average case of diabetes reflect most clearly the inroads of this affection, as well as the patient's behavior under the stress thereby imposed. Of this we have ample proof, in numerous patients in whom repeated examinations were made, over extended periods of time. In this connection also, the opsonin test, hitherto studied only in its relation to infectious processes, should be useful in the investigation of several other conditions—gout, rickets jaundice, and cachexias consequent to chronic nephritis, hepatic cirrhosis, malignant disease, and severe anemia.